PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	Fein
Serial No.	09/919,102
Filed	July 31, 2001
Art Unit	1653
Confirmation No.	2446
Examiner:	Fernandez
Title	**SELECTIVE ENZYME TREATMENT OF SKIN CONDITIONS**
Atty. Docket No.	HOFE 02

Cincinnati OH 45202 January 24, 2007

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF HOWARD FEIN, M.D.
PURSUANT TO 37 C.F.R. §1.132

I, HOWARD FEIN M.D., declare as follows:

1. I am the named inventor in the above-identified patent application.

2. I hold a Doctor of Medicine from the University of Southern California School of Medicine. I have over seven years of experience in dermatology and treatment of skin conditions, which is the subject of the application. I have read the Office Action of September 28, 2006 and understand the Examiner's position.

3. My method selectively removes a seborrheic keratosis condition from skin using trypsin. A formulation containing trypsin as the sole active agent is applied to skin at the site of the seborrheic keratosis. One or more applications are used within at least 18 minutes. Multiple applications may also be used, such as one or two applications a day, or one to ten applications a day. Because none of Klein, Fortney, or SU Patent 1685448, alone or combined with Zaias, Rawlings, or Burbach, teach or suggest or motivate a method using trypsin to treat seborrheic keratosis, and in which the parameters (time, concentration, etc.) for applying the enzyme is selected for the patient's particular situation, I disagree with the Examiner that each of these references renders my invention obvious.

4. As I understand the Examiner requested during the January 9, 2007 personal interview with my patent attorney, I provide a description of seborrheic keratosis, as known to one skilled in the art and supported

at least in "Histopathology of the Skin", Lever and Schaumburg-Lever, 1983, pp. 476-482 (J.B. Lippincott Company, Philadelphia, PA), a copy of which is attached.

5. Seborrheic keratosis is a pathological skin tumor, referred to as a neoplasm (as recognized by one skilled in the art, pathology does not imply malignancy). The new growth is a lesion that is sharply demarcated, brownish in color, and slightly raised. The lesion may have a smooth or verrucous surface, but it characteristically shows keratotic plugs. The size of the lesion ranges in size from a few millimeters to several centimeters in diameter.

6. There are six general types of seborrheic keratoses. These are acanthotic, hyperkeratotic, reticulated, clonal, irritated, and melanoacanthoma. A single lesion may contain one type, or may contain more than one type. All types, however, have hyperkeratosis, acanthosis, and papillomatosis. Acanthosis is due entirely to the upward extension of the tumor, manifest as a raised lesion on a skin surface. The acanthotic type is the most common of seborrheic keratosis.

7. There are two types of cells in the acanthotic epidermis. The first cell type has the appearance of squamous cells that are normally found in the epidermis. The second cell type has the appearance of basaloid cells that resemble basal cells found in the basal layer of the epidermis; upon histologic examination, areas of edema and intercellular bridges can be seen. Thus, the seborrheic keratosis lesion has a cellular layer resembling the epidermis.

8. As described in the Lever and Schaumburg-Lever reference, all six types of seborrhic keratoses affect the epidermal layer of the skin.

9. One embodiment of my method treating seborrheic keratosis is described in Example 1, page 22, of my application. A composition consisting of 2.5% trypsin is applied to a lesion (as shown in my Fig. 1) six times at intervals of three minutes. The timing and number of intervals can be varied according to the size of the lesion. Erosion was present at the treatment site following the protocol (Fig. 2). The treated area was washed and dressed. No other treatment was applied. At three weeks the lesion was eliminated without scarring (Fig. 3). At six months the treated area appeared the same as the surrounding unaffected skin areas (Fig. 4).

10. The SU Patent 1685448 discloses a treatment protocol of applying, for up to two days, an ointment containing trypsin and other components. There is no indication of how many times the ointment was applied during this time. The ointment also contained dimethylsulfoxide (DMSO) at a concentration that effects enzyme activity. I described this in my August 15, 2005 Declaration.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under §1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the subject application or any patent issued thereon.

Date	Howard Fein, M.D.